GENERAL HEADQUARTERS
UNITED STATES ARMY FORCES, PACIFIC
OFFICE OF THE CHIEF SURGEON

A.P.O. 500
16 November 1945

CIRCULAR LETTER)
:
NO . . . . . 51)

DIPHTHERIA

1. Introduction. Reliable information upon the incidence of communicable diseases prevalent in areas now occupied by United States troops indicates that diphtheria is sufficiently widespread to constitute a hazard to occupation forces. War Department Technical Bulletins Medical Numbers 47 and 143 deal with diphtheria in considerable detail; however, in view of the urgent importance of controlling the spread of diphtheria and treating it promptly and the possibility that all medical officers have not seen these publications this circular has been prepared.

2. Diphtheria. Paragraph 5, WD TB MED 47, Subject: "Control of Diseases of Respiratory System and Other Diseases Transmitted by Discharge from Respiratory Tract", dated 28 May 1944, is quoted:

"5. DIPHTHERIA. a. Recognition of disease. An acute infectious disease characterized by the development of dirty white or grayish patches of pseudomembrane on the mucosa of the respiratory tract, with damage to other organs and tissues, particularly the heart and nerves, caused by toxin absorbed from the local lesions. The onset is almost always insidious and the febrile response moderate. Lesions of the tonsils, soft palate, and pharynx are most commonly seen. Mechanical obstruction to breathing associated with laryngeal diphtheria is uncommon in persons of military age. In nasal diphtheria, a serosanguineous discharge may be the only symptom. Such cases are frequently unrecognized and are dangerous sources of infection. Diphtheritic infections of wounds and mucous surfaces other than the respiratory tract have occurred with unexpected frequency in some active theaters of operations. The diphtheritic membrane adheres firmly to the underlying tissue and when separated leaves a bleeding surface. The clinical diagnosis of diphtheria should always be confirmed by cultivation of the organism from the lesions and subsequent identification.

"b. Etiological agent. Diphtheria bacillus, Corynebacterium diphtheriae (Klebs-Loeffler bacillus).

"c. Source of infection. Discharges from diphtheritic lesions and secretions from the respiratory tract of cases and carriers.

"d. Mode of transmission. By direct contact with a case or carrier or indirectly by articles freshly soiled with discharges from such individuals; occasionally through contaminated milk or milk products.

"e. Incubation period. Usually 2 to 5 days.

"f. Period of communicability. Variable; depends upon the presence of the virulent organisms in discharges from the lesions or secretions of cases and carriers. In patients with diphtheria the infectious period is usually about 2 weeks from onset. It seldom exceeds 4 weeks. In the majority of carriers the organisms persist in the pharynx for approximately the same period as in convalescent cases. Occasionally, chronic carriers may harbor virulent organisms for several months.

"g. Susceptibility and immunity. Susceptibility may be determined by the Schick test. Children and adults apparently develop immunity in proportion to their contact with persons who are carriers of diphtheria bacilli. It is estimated that approximately 50 per cent of persons of military age are susceptible. Immunity following an attack is usual, but not invariable. Active immunity can be induced by the injection of diphtheria toxoid. Diphtheria may occur occasionally in individuals who have previously had the disease or who have received injections of toxoid. The prophylactic use of diphtheria antitoxin (passive immunization) is not recommended except under exceptional conditions. On the rare occasions when its use is deemed advisable, the dose for adults should be 2,000 units of diphtheria antitoxin administered subcutaneously.

"h. Prevalence. Endemic in the temperate and subtropical zones with irregularly occuring periods of epidemicity. Contrary to common belief, experience now shows that epidemics of diphtheria may occur in the tropics. The highest prevalence is during the fall and winter months. In areas where an active program of immunization has been carried out, the disease has become sporadic. In the absence of active public health measures, however, the incidence may increase greatly.

"i. Methods of control. (1) Recognition of disease. Clinical symptoms with bacteriological confirmation.

(2) Isolation of patients. Until three cultures from the nose and three from the throat, taken at least 24 hours apart, are negative for diphtheria bacilli. In the event that cultures are repeatedly positive, isolation may be terminated, when, following appropriate testing, the organisms have been shown to be avirulent. If facilities for bacteriological control are not available, the patient should be isolated for a period of 3 weeks from the time of onset.

(3) Concurrent disinfection. Discharges from the respiratory tract or lesions elsewhere, and articles contaminated with such discharges.

(4) Terminal disinfection. Thorough cleaning.

(5) Quarantine of contacts. None.

(6) Physical inspection. Upon the occurrence of a single case of diphtheria in a company or other unit of comparable size, physical inspection of contacts should be carried out by a medical officer daily for 5 days following the last exposure. Inspection should include examination of the nose and throat. If a second case occurs within 2 weeks, daily inspection should be resumed, and in addition, Schick tests should be carried out on the entire company with nose and throat cultures on food handlers who are contacts and on occupants of the same quarters in which cases have occurred. From the results of Schick tests and nose and throat cultures, certain groups may be selected which may be treated as indicated in the following table:

Schick reaction	Disposition
Positive	Start active immunization. (See (9) below.)
Combined	Do not immunize, or else begin with small doses of toxoid.
Negative or pseudo . .	Do not immunize.

Individuals with positive or combined Schick tests and positive cultures are potential cases and should be watched with special care. Those with negative or pseudo Schick tests and positive cultures are carriers (see (7) below). All individuals with positive cultures should be isolated as prescribed in section IV, AR 40-210. One or even two negative cultures are not conclusive evidence that an individual is not harboring diphtheria bacilli.

(7) Carrier control. Before releasing carriers from isolation, negative cultures should be required as stated in paragraph 15 d (3), sec IV, AR 40-210. If cultures have not become negative within 4 weeks, consideration should be given to the removal of tonsils and adenoids or other appropriate treatment. Antitoxin is of no value in the treatment of carriers.

(8) Protection of attendants. No persons should be permitted to act as attendants for diphtheritic cases or carriers unless known to be immune.

(9) Active immunization. Immunization of military personnel against diphtheria is not a routine procedure and should be undertaken only when in the opinion of the responsible medical officer a definite hazard from this disease exists. The procedure ordinarily recommended is the subcutaneous injection of four doses (0.1 cc, 0.5 cc, 1.0 cc and 1.0 cc, respectively) of diphtheria toxoid, plain, at intervals of approximately 3 weeks. Reactions to diphtheria toxoid are not uncommon in adults, particularly in those who show the combined type of reaction to the Schick test. For this reason, only those individuals who have been shown by the Schick test to be susceptible should be immunized. For individuals demonstrating combined reactions to the Schick test and for those with a history of reaction to previous injection of diphtheria toxoid, the individual dose may be divided into a series of graduated doses and administered over a period of several days.

(10) Schick reaction. The test dose consists of 1/50 m.l.d. of diphtheria toxin in a volume of 0.1 cc, and is injected intracutaneously. A control consisting of inactivated toxin should always be injected in the opposite arm, in order to determine whether the individual is hypersensitive to products of the diphtheria bacillus. The reactions should be read if possible at 48 hours and always on the fourth or fifth day. Hypersensitivity reactions are more marked at 48 hours than later. A true positive Schick reaction, however, does not usually reach its maximum intensity until about 96 hours following injection.

(a) Negative reaction. No erythema occurs, indicating the presence of immunity.

(b) Positive reaction. An area of redness begins at the site of injection of the active toxin after 24 to 36 hours. The maximum intensity is reached at about 96 hours, with subsequent slow fading. No reaction occurs at the site of the control injection. A positive reaction indicates susceptibility to diphtheria.

(c) Pseudo-reaction. A reaction occurs at the site of injection of both the active and inactivated toxin usually within the first 24 hours, fading more rapidly than a true positive Schick reaction. If the reaction to the control is as great as to the active toxin, the individual is ordinarily immune to diphtheria but is hypersensitive to associated substances present in the solution.

(d) Combined reaction. A reaction occurs to both the control and active toxin, but, unlike the pseudo-reaction, that to the active toxin is more marked than the control at 96 hours. The combined reaction indicates susceptibility to diphtheria combined with hypersensitivity to the bacterial products. In individuals who show a combined reaction, immunization with diphtheria toxoid should be approached cautiously, since severe reactions to the immunizing dosage occur most frequently in this group.

(11) Investigation of the source of infection. (See (6) above.)"

3. Technique of Obtaining Nasopharyngeal Swab. Laboratory Methods of the United States Army, 1944, 5th Edition, Gentzkow, p. 507, is quoted:

"From suspected clinical cases of diphtheria, collect a portion of the pseudomembrane with forceps or by means of a cotton swab. If membrane formation is absent, or in the case of examination for carriers, swab over the mucous membranes of the pharynx, tonsils, nasal cavities and auditory canals. In the collection of the specimen, avoid contamination if possible by not allowing the swab to touch the tongue or any part of the oral cavity, or to come in tontact with excessive nasal or pharyngeal secretions."

4. Treatment of Nasopharyngeal Diphtheria.

a. General. Because of the danger of diphtheritic myocarditis, bed rest of from four to six weeks duration is an essential part of treatment. After the first day or two drugs to overcome pain and prevent restlessness are usually unnecessary. During the stage of sore throat a liquid diet is all that will be tolerated comfortably but when soreness of the throat disappears normal feeding is permissible. The possible need for correcting obstruction of the air passages by suction, intubation or tracheotomy must be anticipated and appropriately prepared for in every case of nasopharyngeal diphtheria.

b. Specific. Diphtheria antitoxin is a lifesaving therapeutic measure when indicated and the need for it is one of the most important of medical emergencies. Success in the treatment of diphtheria is directly proportional to the speed with which antitoxin is given after the onset of infection. Therefore, when physical findings in the upper air passages are sufficiently suggestive of diphtheria, antitoxin should not be withheld until the completion of cultural studies. There is difference of opinion regarding the quantity of antitoxin that should be given but the following general recommendations are offered:

(1) Mild constitutional reaction with diphtheria confined to the nasopharynx on the first or second day of the disease: 20,000 units intramuscularly.

(2) Severe constitutional reaction: 50,000 units, half intramuscularly and half diluted with 200 cc. normal saline intravenously.

(3) For each day elapsing between the onset of infection and the administration of antitoxin add 20,000 units and give half intramuscularly and half intravenously. The greatest possible care must be exercised according to accepted practice to guard against serious anaphylactic reactions to the injection of antitoxin. In the event that desensitization to antitoxin proves necessary as a result of appropriate skin testing for sensitivity, the administration of 25,000 units of penicillin every three (3) hours may be of value until desensitization has been accomplished. Penicillin is in no sense a substitute for antitoxin which must be administered in full doses as soon as it can safely be done.

5. Cutaneous Diphtheria. (WD TB MED 143, dtd February 1945, abstract is reproduced).

a. General. The fact that virulent diphtheria organisms may infect both wounds and skin lesions is often uncommon knowledge to medical officers. As this information becomes more universally known, there will be a greater recognition on the part of our medical officers of instances of cutaneous diphtheria which otherwise would have been overlooked. The diagnosis requires adequate and experienced laboratory aid. Neuritis and myocarditis of undetermined cause, may be a sequel to unrecognized cutaneous diphtheria. For these reasons, this subject is worthy of serious consideration.

b. Definition. As a standard, all-inclusive definition, the term "cutaneous diphtheria" is used in reference to any lesion of the skin from which Corynebacterium diphtheriae of proven virulence is recovered.

c. Epidemiology. From a study of possible contact infections, a definite epidemiological relationship has been established between cutaneous and pharyngeal diphtheria. Either type may be either a primary or secondary infection of the other.

d. Clinical Features.

(1) Systemic reaction. In general, there is none. Infrequently symptoms of fever and prostration occur due to infection of the skin lesion with bacteria other than the diphtheria organisms.

(2) Types of skin lesions. The infection is characterized by an eruption evidenced by gray ulcerating patches developing at the site of the skin lesion. Lesions occur most frequently on the extremities of the body. In addition, they may occur in any portion of the body, in the genitals of both sexes, in the axillary and postauricular regions, in the conjunctivae, on the digits, on the lips, as a post-operative complication, and as sequelae of bruises and injuries. The lesion is an ulcer of varying size, single or multiple, indurated, deep, and "punched out", with a sharply defined margin. Virulent diphtheria bacilli invade relatively superficial lesions as well as deeper wounds.

e. Complications.

(1) Neuritis. The incidence of post-diphtheritic peripheral neuritis in troops has been underestimated. Symptoms and signs of neuritis appear most frequently in the lower extremities.

(2) Myocarditis. Significant electrocardiographic changes have become evident in studied cases of cutaneous diphtheria.

f. Diagnosis.

(1) General. The diagnosis of cutaneous diphtheria depends first upon thinking of it as a possibility. Suspicion of diphtheria cannot be confirmed and final diagnosis of diphtheria is not justified unless virulent organisms are recovered or the patients develop characteristic neuritis or myocarditis. Keen alertness and cooperation on the part of both clinician and laboratory officer are essential.

(2) Clinical. The actual presence of infection with diphtheria organisms can be established only by laboratory proof (see (1) above). However the medical officer must often act promptly in instituting isolation and treatment.

(a) Experience indicates that the indurated, round, and "punched out" type of ulcer is the lesion most likely to be infected.

(b) Suspicion of cutaneous diphtheria is increased in the following instances:

1. A single patient with the typical type ulcer.

2. A group of patients with suspected ulcers, originating in a common area.

3. Proof of diphtheria in one or more patients with skin disease or in individuals associated with such patients by development of clinical evidence of pharyngeal or nasal diphtheria or appearance of characteristic complications of diphtheria. The time of appearance of characteristic complications varies.

(c) A knowledge of the endemicity or epidemicity of diphtheria is most important. When diphtheria is known to be endemic, patients with ulcers should be regarded as potentially having diphtheria and isolated until they are proven to be non-diphtheritic. Where diphtheria is epidemic, not only such patients but also patients with exfoliative and eczematoid lesions should be managed in this way.

(3) Laboratory Study. (See par. 306, TM 8-227)

(a) The Corynebacterium diphtheriae is a Gram-positive, non motile rod which may manifest marked pleomorphism, determined in part by the age of the culture and the constituents of the medium. The most typical morphology is seen in films made from Loeffler slant cultures stained with Loeffler's methylene blue. The rods may be straight or curved and occur in aggregates of peculiarly angled clusters. There may be central or terminal swelling and the frequent irregular staining occasionally produces a granular or beaded appearance. The longer rods generally have this appearance, whereas the shorter rods stain deeply and uniformly. When the characteristic morphology is noted in a film from an initial Loeffler slant or a suspected lesion, it may be considered as presumptive evidence for the presence of C. diphtheriae.

(b) Direct smears. The heavy contamination of most skin lesions, and especially those of field soldiers, by numerous bacteria makes this method of examination rarely of value. Nevertheless, it should be employed in suspected cases, since large numbers of organisms with all the morphological characteristics of C. diphtheriae are found occasionally.

(c) Cultural procedure. Loeffler's medium is the most widely employed preparation for the cultivation of Corynebacteria. Adequate growth is usual in 12 to 18 hours, in the form of small, moist, grayish, shiny colonies. After such incubation, the entire growth should be emulsified on the slant. A methylene blue stained film is prepared and examined for C.diphtheriae and a plated medium is streaked. Transfers are made from suspicious colonies on the plate to Loeffler's slants. Such slant cultures are used for further study of the morphology of the suspected organisms, and for fermentation and animal virulence studies.

(d) Fermentation of carbohydrates. C. diphtheriae will generally ferment dextrose and not sucrose in 5 days at 37° C. Cultures

of organisms with such properties are used for animal virulence tests.

(e) Virulence determination. The reaction of experimental animals to the inoculation of suspected diphtheria organisms is the only certain method of determination. The single animal method of Fraser using the rabbit or guinea pig is recommended. Animal virulence is not directly related to any specific colony morphology or biochemical reaction.

g. Treatment.

(1) Isolation. See paragraph h (2).

(2) General. Skin lesions which contain diphtheria organisms should be managed in accordance with generally accepted therapeutic principles for dermatological diseases. Care should be taken to avoid overtreatment. Diphtheria organisms usually disappear rapidly from skin lesions once bed rest and general and local care are instituted. Patients with diphtheria of the skin are subject to all the complications that may develop in the nasopharyngeal form of the disease. Accordingly, these complications should be guarded against and treated promptly in case they appear.

(3) Local. The lesion should be thoroughly cleaned. The application of steril warm saline compresses is recommended. Such treatment, combined with general care, usually suffices to clear the lesion of diphtheria organisms, but compresses soaked in penicillin solution (250-500 Oxford units per cc) give a quicker effect. The parenteral administration of penicillin has also been suggested. Applications of various ointments, dyes, and sulfonamides are of no value and may be harmful. Sulfonamides are also ineffectual when given by mouth.

(4) Specific. When it is decided after careful epidemiologic and clinical consideration that a patient probably has cutaneous diphtheria, antitoxin should be given without delay. If a clinical diagnosis is not justified, the results of laboratory studies should be awaited. In cases in which only cutaneous lesions are infected and no complication is present, the recommended amount is 20,000 units, administered intramuscularly in a single dose. The usual precautions to prevent anaphylactic reactions to foreign proteins must be rigidly employed. Further administration of antitoxin in such cases must depend upon the clinical findings and course. It is to be noted that there is no evidence that antitoxin hastens the healing of skin lesions. Patients with nasopharyngeal diphtheria as well as cutaneous diphtheria should be treated according to the usual principles for the management of nasopharyngeal diphtheria.

h. Control.

(1) General. The administrative procedures prescribed in AR 40-210 for the control of diphtheria are applicable to the cutaneous form of the disease. In applying these procedures, the following considerations should be borne in mind:

(a) Individuals known to harbor or strongly suspected of harboring C. diphtheriae in cutaneous lesions, even though not exhibiting symptoms or signs of clinical diphtheria, should be considered to be carriers and isolated accordingly.

(b) Contacts to cases of cutaneous diphtheria should be subjected to the same inspections and administrative control as contacts to nasopharyngeal diphtheria.

(c) Stations receiving troops, who may have been exposed to cutaneous diphtheria, should be alert to the possibility of faucial or cutaneous diphtheria developing among such troops.

(2) Isolation. Strict isolation technique should be employed in the same manner for cutaneous diphtheria as for the nasopharyngeal type. This isolation should be continued until three cultures from the lesion and from the nose and throat, taken at least 24 hours apart, are negative for diphtheria bacilli except that the isolation may be terminated if, by appropriate tests, the organisms are found to be avirulent.

(a) Particular attention should be given to the disinfection of dressings and other articles contaminated with discharges from the lesions. Since virulent C. diphtheriae have been recovered from the floor of a cutaneous diphtheria ward, special care must be taken in the proper cleansing and disinfection of the floors in rooms or wards in which these patients are being treated. Under no conditions should dry sweeping be allowed.

(b) No person should be permitted to act as attendants for cases of cutaneous diphtheria unless known to be Schick negative.

(3) Immunization. (See TB MED 114)

(a) Immunization of large groups of military personnel to diphtheria is not a routine procedure. It should be undertaken only under special circumstances. While it is apparent that immunity to diphtheria toxin does not prevent the multiplication of diphtheria organisms in skin lesions, such immunity should prevent systemic damage from the toxin elaborated by these organisms. In addition, since cutaneous diphtheria may be a source of nasopharyngeal infection, immunization may be indicated for the prevention of an outbreak of the latter type of disease. It is considered that the incidence of susceptibility in United States troops is such that, with extensive exposure, considerable numbers of diphtheria cases may develop. Therefore, under some conditions, active immunization may be indicated. The decision for or against the application of this measure is one requiring sound medical judgement and must, in each instance, be based on a careful evaluation of the problem at hand. The following are offered as tentative indications for such immunization. They are intended as guides only since they may not be applicable to all situations.

1. Admission rates for diphtheria (either or both forms) above 100 per thousand per annum when averaged over a period of several weeks except that

2. When the disease is limited to small organizations or units, that is, 1,000 strength or less, the critical rate might well be considered to be 200 per thousand per annum and

3. In large organizations, that is 20,000 or more, the critical rate might be considered to be 50 per thousand per annum or less in the presence of persistently occurring cases, scattered throughout the organization.

4. Situations in which admission rates are not considered reliable but in which there is definite indication of the spread of diphtheria in the organization or command concerned.

(b) The recommended method for immunization of adults to diphtheria. (See paragraph 5 i (9), WD TB MED 47, quoted in paragraph 2).

(4) Schick testing. The conduct of Schick test surveys of large groups of military personnel is not considered to be a practical procedure, particularly under field conditions. Accordingly, this procedure should not be used as a control measure unless it is possible to carry it out very carefully, using materials that are known to have been stored under proper conditions, and there is opportunity for reading of reactions at 48 and 96 hours.

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